

REMARKS

The July 30, 2002 Official Action and the references cited therein have been carefully reviewed. In view of the following remarks, favorable reconsideration and allowance of this application are respectfully requested.

At the outset, Applicant's note that the Examiner has indicated that claims 15-22 are allowable.

At page 2 of the Official Action, the Examiner has rejected claims 1-14 under 35 U.S.C. §103(a) as allegedly unpatentable over U.S. Patent 5,371,017 to Houghton et al., in view of Suzich et al (1993). It is the Examiner's position that one of ordinary skill in the art would have been motivated to apply the teaching of full length, native recombinant expression of HCV NS3 to produce an enzyme comprising amino acids 1027-1657 because Suzich et al. teach that these amino acids define the NS3 gene product. The Examiner further states that it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to produce and use the claimed HCV NS3 proteins.

Applicants respectfully submit that the present claims are in condition for allowance. The above-noted rejection under 35 U.S.C. §103 is, therefore, respectfully traversed.

CLAIMS 1-14 ARE NOT RENDERED OBVIOUS BY THE COMBINED DISCLOSURES OF THE '017 PATENT AND SUZICH ET AL.

Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness on claims 1-14 of the present application over '017 patent in view of Suzich et al. It is stated in M.P.E.P. §2142:

To establish a *prima facie* case of

obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure.

However, in the instant case, none of the three basic criteria to establish a *prima facie* case of obviousness have been met. More specifically, claims 1-14 of the present invention are directed to a native, authentic enzymatically active NTPase/RNA helicase protein produced by expressing in an eukaryotic expression system a NTPase/RNA helicase protein from Hepatitis C virus (HCV) comprising amino acids 1027-1657, and wherein the NTPase/RNA helicase protein is purified under conditions where the enzymatic activity thereof is maintained. On the other hand, '017 patent discloses a DNA construct encoding 151 amino acids of the SOD protein fused to amino acids 946-1630 of HCV NS3 protein. This fusion protein is expressed in E.coli and purified under denaturing and renaturing conditions. Accordingly, '017 patent fails to suggest or teach all the claim limitations of claims 1-14 of the present invention. More importantly, these omitted claim limitations are neither suggested nor taught by Suzich et al. Suzich et al teaches a DNA construct encoding a HCV protein comprising amino acids 1193-1657. Again, this recombinant HCV protein is expressed in E.coli and purified under denaturing

and renaturing conditions. The Examiner asserts that '017 patent has disclosed a "DNA construct encoding the entire NS3 domain" at lines 18-55 of column 4, and various well-established recombinant expression means in the art, including both expression of fusion proteins and nonfused proteins at lines 6-16 of column 10. The Examiner further asserts that Suzich et al discloses the entire HCV NS3 genes product as residing in amino acids 1027-1657 of the HCV polyprotein. Again, the teachings of '017 patent and Suzich et al, considered alone or in combination, has failed to suggest or teach all the claimed limitations of claim 1-14. More specifically, '017 patent and Suzich et al, each alone or in combination, fails to suggest or teach the expression of NTPase/RNA helicase protein of HCV in an eukaryotic expression system and the purification of NTPase/RNA helicase protein of HCV under conditions where the enzymatic activity thereof is maintained.

More over, the presently claimed enzyme has both NTPase activity **and** helicase activity. While the investigators of '017 patent and Suzich et al demonstrate that residues 1193-1657 had NTPase activity, they report at page 6156, second column, third line: "To our knowledge, there are no reports describing the putative RNA helicase activity for these proteins of viruses of the *Flaviviridae*." Thus, this reference provides no teaching or suggestion that the helicase activity of HCV resides in residues 1027-1657. More importantly, although '017 patent mentions in passing the expression of a recombinant protein comprising amino acids 1027-1657 of NS3 from HCV, it fails to provide evidence supporting that such a recombinant protein will maintain a comparable NTPase activity as the recombinant protein comprising amino acid 946-1630. Therefore, there is no suggestion or motivation in the cited

references to combine the teachings of '017 patent and Suzich et al. Furthermore, a reasonable expectation of success to combine '017 patent and Suzich et al has not been provided by the cited references.

It is noted in passing that Chiron, the owner of '017 patent has filed U.S. Patent Application No. 08/529,169, now U.S. Patent No. 6,194,140. The '140 patent includes claims directed to a truncated helicase protein and helicase assays for testing compounds for activity against hepatitis C virus. Apparently, Chiron did not believe that the disclosure in the '017 patent was sufficient to support claims to a helicase and assays therewith to identify anti-HCV agent. Otherwise the patent application directed to the above mentioned subject matter would not have been filed. It is further noted in this regard, that the present Applicants have provided evidence demonstrating concept and reduction of the instantly claimed invention prior to the filing date of the patent application which was ultimately issued as the '140 patent. See the declaration of Dr. Collett, submitted with Applicants' amendment dated September 26, 1997 in connection with the prosecution of the parent application 08/678,771.

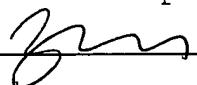
In light of all the foregoing, Applicants respectfully submit that claims 1-14 of the present application are patentable over the combined disclosures of '017 patent and Suzich et al. Accordingly, Applicants request that the rejection of claims 1-14 under 35 U.S.C. §103 be withdrawn and the present application be passed to issue. In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to telephone the undersigned attorney at the phone number give

below.

Respectfully submitted,

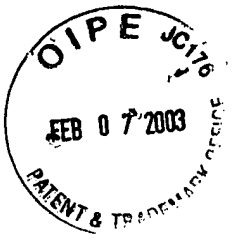
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MARKED-UP VERSION SHOWING CHANGES

In the specification:

At page 1, line 1-2, please replace the existing title
"METHODS FOR IDENTIFYING INHIBITORS OF HELICASE C VIRUS" with
the following:

--METHODS FOR IDENTIFYING INHIBITORS OF HELICASE ACTIVITY
FROM HEPATITIS C VIRUS--